REMARKS

Applicant wishes to thank Examiner Lucas and Supervisor Housel for the courtesy extended to Nancy Vensko, attorney of record, on September 13, 2004. The interview Summary Form PTOL-413 summarizes the discussions held at the personal interview. The present response to the outstanding Office Action includes the substance of the Examiner Interview.

A. Disposition of Claims

The invention is related to the complete nucleotide sequence of the core gene of 52 HCV isolates that represent 14 genotypes, the core gene sequences of 9 genotypes having not been previously reported (i.e., genotypes 2c, 4a-f, 5a and 6a). By this amendment, Applicant has amended Claims 4, 5, 15, 16, 19, 32, 37, 38, and 46. Applicant has cancelled Claims 1-3, 6-10, 17-18, 20-31, 45, and 47-58 as being drawn to non-elected restriction groups (and Claim 59 as being redundant to Claim 39). Thus, Claims 4, 5, 11-16, 19, 32 -44, and 46 are pending. This amendment is presented to make explicit that which was implicit in the pending claims and/or to read on the elected species of the core protein of SEQ ID NO: 206 and peptides thereof (see Office Action at ¶ 3), and thus for reasons unrelated to patentability. Support for the amendment is found throughout the specification, for example as indicated below. No new matter has been added. Reexamination and reconsideration of the applications, as amended, are respectfully requested.

B. Compliance with Sequence Listing under 37 CFR 1.821 (d)

The issue is whether the specification is in compliance with 37 CRF 1.821(d). The rule is that patent applications that contain disclosures of sequence must disclose the sequence in a Sequence Listing, assign the sequence a SEQ ID NO, and refer to the sequence in the text by SEQ ID NO even if the sequence is also embedded in the text. Additionally, under MPEP 2422.02, where the sequence is represented in a figure, the SEQ ID NO must still be used, either in the drawing or in the Brief Description of the Drawings. Here, although sequences are represented in the figures (the consensus sequences), the SEQ ID NOs are used in the drawings and thus are not required to be used in the Brief Description of the Drawings (pages 8-16). Additionally, under MPEP 2422.03, the disclosure must refer to the sequence in the text by SEQ ID NO even if the sequence is also embedded in the text. Here, the sequences are not embedded in the text (the consensus sequences on page 57) but are represented in the figures (as specifically referenced on page 57), and the SEQ ID NOs are used in the drawings themselves, thus under the doctrine of incorporation by reference the SEQ ID NOs are not required to be used in either the

Brief Description of the Drawings or the text because the SEQ ID NOs are used in the drawings. Moreover, the parent, USP 5,882,852 issued under this doctrine of incorporation by reference. Finally, putting SEQ ID NOs into the text would maximize confusion and thus violate the policy to minimize confusion stated in MPEP 2422.02. The conclusion is that the specification is in compliance with 37 CRF 1.821(d).

C. Compliance with MPEP 2173.05(s)

The issue is whether the claims are in compliance with MPEP2173.05(s). The rule is that incorporation by reference in a claim to a figure or table is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Here, reference in the claims to the figures has been deleted, except for claims 32 and 38, because, as discussed below, there is no practical way to define genotype-specific as belonging to a single genotype of HCV (claim 32) or universally conserved as belonging to all genotypes of HCV (claim 38) except by reference to Figure 7J. The conclusion is that the claims are in compliance with MPEP 2173.05(s).

D. Compliance with 35 USC 112, second paragraph

The issue is whether Claim 32 and claims dependent thereon and Claim 38 and claims dependent thereon are in compliance with 35 USC 112, second paragraph. The rule under MPEP 2173.02 is that definiteness must be analyzed not in a vacuum but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Here, genotype-specific has been defined as belonging to a single genotype of HCV (claim 32) and universally conserved as belonging to all genotypes of HCV (claim 38) with reference to Figure 7J. Support for the definitions is found throughout the patent specification, for example, at original claim 33 "a single genotype of HCV" and at original claim 39 "all genotypes of HCV". This is because, as stated in the Brief Description of the Drawings at 15:19-22, Figure 7J shows the alignment of the consensus sequences of the genotypes of HCV to produce a consensus sequence for all genotypes. As continued in the Brief Description of the Drawings at 15:30-34, the amino acids shown in capital letters in the consensus sequence shown in Figure 7J are conserved among all genotypes while the amino acids shown in lower case letters represent amino acids found most frequently in the sequences aligned to produce this consensus sequence. In the previous Response to Restriction

Requirement, Applicant noted that the chart on page 57 shows examples of domains from which genotype specific peptides may be *deduced* (per specification at 56:34), and that the chart on page 59 shows examples of domains from which universally conserved peptides may be *deduced* (per specification at 59:26). In conformance with this explanation, the claims have been amended to define the terms "genotype-specific" and "universally conserved" unambiguously because universally conserved peptides could be *deduced* by one of ordinary skill in the art at the time of the invention from the amino acids shown in capital letters in the consensus sequence shown in Figure 7J while genotype-specific peptides could be *deduced* by one of ordinary skill in the art at the time of the invention from the amino acids shown in lower case in the consensus sequence shown in Figure 7J. Additionally, support for the term "isolated" in claim 32 is found in original claim 32 and support for "isolated" in claim 38 is found in original claim 38. Moreover, support for a size of at least 8 amino acids is found in the specification at 58:14. Finally, a utility is contemplated for both the genotype-specific and universally conserved peptides for the diagnosis of HCV infections (e.g., specification at 58:22-25 and 60:1-3) and for the prevention of HCV infections (e.g., specification at 60:28-33). Several studies in the pre-filing date art had indicated that the three major hydrophilic regions of the C protein contain linear immunogenic epitopes, summarized in Sallberg, M. et al., J. Clin. Microbiol 30: 1989, 1992, attached (see abstract). Per the post-filing date art of Bukh et al., Proc Natl Acad Sci USA 91: 8239, Aug 1994, attached, both universally conserved and genotype specific peptides have implications for the diagnosis, prevention and therapy of HCV infections (see last line), presumably through epitope mapping that is routine as evidenced by Sallberg, M. et al. The conclusion is that, when analyzed not in a vacuum but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made, the claims are definite.

E. Compliance with 35 USC 112, first paragraph

The issue is whether Claims 19 and 46 are in compliance with 35 USC 112, first paragraph. The rule according to MPEP 2164 is that the specification must enable the claims Here, the Patent Office agrees that the specification is enabling for immunogenic compositions. The claims have been amended to conform therewith. The conclusion is that the claims are in compliance with 35 USC 112, first paragraph.

F. Compliance with 35 U.S.C 102

The issue is whether the claims are in compliance with 35 USC 102. The rule according to MPEP 2131 is that to anticipate a claim, the reference must teach every element of the claim. Here, the claims have been amended to make explicit that which was implicit in the pending claims and/or to read on the elected species of the core protein of SEQ ID NO: 206 and peptides thereof (see Office Action at ¶ 3). As explained above and supported in the Brief Description of the Drawings at 15:19-22, and 15:30-34; the claims have been amended to define the terms "genotype-specific" and "universally conserved" unambiguously because universally conserved peptides could be *deduced* by one of ordinary skill in the art at the time of the invention from the amino acids shown in capital letters in the consensus sequence shown in Figure 7J while genotype-specific peptides could be *deduced* by one of ordinary skill in the art at the time of the invention from the amino acids shown in lower case in the consensus sequence shown in Figure 7J. Either the reference does not read on the elected species of the core protein of SEQ ID NO: 206 and peptides thereof. That is, DeLeyes et al. Peptide I is said to read on SEQ ID NO: 180 and PeptideVI to read on SEQ ID NO: 160, Shirai et al. C8 is said to read on SEQ ID NO: 176, and Machida et al. 34 [sic,39]-81 is said to read on Figure 7A-1. None of these is said to read on SEQ ID NO: 206. Or the reference does not read on the genotype-specific or universally conserved peptides as defined in the claims. That is, DeLeyes et al. Peptide II is not universally conserved because it does not read on all capital letters per the attached Exhibit 1, Shirai et al. C7-P10G is not universally conserved because it does not read on all capital letters per the attached Exhibit 2, and neither Ferroni et al. G15V nor R15P is universally conserved because they do not read on all capital letters per the attached Exhibit 3. The conclusion is that the references fail to anticipate the claims, thus the claims are in compliance with 35 USC 102.

G. Compliance with 35 U.S.C. 103

The issue is whether the claims are in compliance with 35 USC 103. The rule according to MPEP 2143 is that the prior art references must teach or suggest all the claim limitations and there must be some suggestion or motivation in the prior art to combine the references. Here, neither primary reference Li et al. nor Takeguchi et al. read on the elected species of the core protein of SEQ ID NO: 206 and peptides thereof. That is, Li et al. F1-H is said to read on Figure 7A and Takeuchi et al. JH to read on SEQ ID NO: 166. Neither of these is said to read on SEQ ID NO: 206. Moreover, the secondary references Liao et al. and Chien et al. cannot fill in the gaps, because the invention is related to the complete nucleotide sequence of the core gene of 52

HCV isolates that represent 14 genotypes, the core gene sequences of 9 genotypes having not been previously reported (i.e., genotypes 2c, 4a-f, 5a and 6a). The missing sequences are empirical and thus nonobvious. The conclusion is that the claims are in compliance with 35 USC 103.

CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

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